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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/978,194	10/15/2001	Avi J. Ashkenazi	GNE.2630P1C10	5226

35489 7590 02/04/2004

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EXAMINER	
KEMMERER, ELIZABETH	

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 02/04/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/978,194	ASHKENAZI ET AL.	
	Examiner	Art Unit	
	Elizabeth C. Kemmerer, Ph.D.	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 September 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *58-70* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *58-70* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *15 October 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)

2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 2/20/02 3/28/02 5/1/03

4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .

5) ☐ Notice of Informal Patent Application (PTO-152)

6) ☐ Other: .

DETAILED ACTION

Status of Application, Amendments, And/Or Claims

The preliminary amendments filed 15 October 2001, 04 February 2002, 26 February 2002 and 03 September 2002 have been entered in full. Claims 1-57 are canceled. Claims 58-70 are under examination.

The Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1646, Examiner Elizabeth C. Kemmerer, Ph.D.

Specification

The disclosure should be reviewed for improper use of active hyperlinks. Active hyperlinks should be deleted from the application.

35 U.S.C. § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 59-63, 66, 67, 69 and 70 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The protein identified as PRO351 is a soluble protein, and is not disclosed as being expressed on a cell surface. Accordingly, the limitation that the claimed protein

comprises an "extracellular domain" is indefinite, as the art does not recognize soluble proteins as having such domains. Further, if the protein had an extracellular domain, the recitation of "the extracellular domain"..."lacking its associated signal sequence" is indefinite as a signal sequence is not generally considered to be part of an extracellular domain, as signal sequences are cleaved from said domains in the process of secretion from the cell. Also, it is noted that the specification indicates that PRO351 is a secreted protein, and does not define an extracellular domain for PRO351. See, for example, pp. 12 and 63-64, and Figure 49.

35 U.S.C. §§ 101 and 112, First Paragraph

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 58-70 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a credible, specific and substantial asserted utility or a well established utility.

The claims are directed to isolated polypeptides comprising sequences that are structurally similar to PRO351 (SEQ ID NO: 132 shown in Figure 49). The specification

indicates that PRO351 is a new member of the prostasin family based on the structural similarity between PRO351 and prostasin. The specification asserts that PRO351 would have properties and activities typical of the prostasin family (p. 162). Since human prostasin is expressed in prostate tissue, the specification also asserts that PRO351 is of interest for the study, diagnosis and treatment of medical conditions involving the prostate. These asserted utilities are not substantial. The structure, tissue-specific expression pattern and cellular localization of human prostasin have been disclosed in the prior art (Yu et al., 1996, J. Biol. Chem. 270:13483-13489). However, the physiological functions of prostasin were not disclosed, nor was its physiological substrate (p. 13483, right column, end of first partial paragraph). Therefore, based on the disclosure in the specification and the prior art, one skilled in the art would not know how to use PRO351 or human prostasin without resorting to significant further research to determine the physiological roles and substrates of these polypeptides, and thus the asserted utility is not substantial. Additionally, the structural similarity between PRO351 and human prostasin is very low, only about 14% (see Appendix A). Therefore, it is not clear that PRO351 is truly a new member of this gene family.

The specification also discloses that PRO351 tested positive in 10 out of 19 lung tumor samples in a gene amplification assay at pp. 331-346. While this establishes a utility for the PRO351 gene (SEQ ID NO: 131), it does not establish a utility for PRO351 polypeptides or antibodies. The art demonstrates that gene amplification does not

reliably correlate with increased mRNA transcript levels or increased polypeptide levels. Pennica et al. (1998, PNAS USA 95:14717-14722) disclose that,

> "An analysis of *WISP-1* gene amplification and expression in human colon tumors showed a correlation between DNA amplification and overexpression, whereas overexpression of *WISP-3* RNA was seen in the absence of DNA amplification. In contrast, *WISP-2* DNA was amplified in the colon tumors, but its mRNA expression was significantly reduced in the majority of tumors compared with the expression in normal colonic mucosa from the same patient."

See p. 14722, second paragraph of left-hand column; pp. 14720-14721, "Amplification and Aberrant Expression of *WISPs* in Human Colon Tumors". See also Konopka (Proc. Natl. Acad. Sci. (1986) 83:4049-4052), who state that

> "Protein expression is not related to amplification of the abl gene but to variation in the level of bcr-abl mRNA produced from a single Ph1 template" (see abstract).

Finally, even if gene amplification correlates with increased transcription, it does not always follow that protein levels are also amplified. See Haynes et al. (1998, Electrophoresis 19:1862-1871), who studied more than 80 proteins relatively homogeneous in half-life and expression level, and found no strong correlation between protein and transcript level. For some genes, equivalent mRNA levels translated into protein abundances which varied more than 50-fold. Haynes et al. concluded that the protein levels cannot be accurately predicted from the level of the corresponding mRNA transcript (p. 1863, second paragraph, and Figure 1). Therefore, the art indicates that it is not the norm that gene amplification, or even increased transcription, results in increased protein levels.

Therefore, the asserted utility is not substantial, as the real-world use has not been established. Thus, the proposed use of the PRO351 polypeptides are simply starting points for further research and investigation into potential practical uses of the polypeptides. See Brenner v. Manson, 148 U.S.P.Q. 689 (Sus. Ct, 1966), wherein the court held that:

> "The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility", "[u]nless and until a process is refined and developed to this point-where specific benefit exists in currently available form-there is insufficient justification for permitting an applicant to engross what may prove to be a broad field", and "a patent is not a hunting license", "[i]t is not a reward for the search, but compensation for its successful conclusion."

Claims 58-70 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a credible, specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Elizabeth C. Kemmerer, Ph.D., whose telephone number is (703) 308-2673. The examiner can normally be reached on Mondays through Thursdays from 7:00 a.m. to 5:30 p.m. The examiner can also normally be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, Ph.D., can be reached on (703) 308-6564.

Official papers filed by fax should be directed to (703) 308-4242. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Elizabeth C. Kemmerer

ELIZABETH KEMMERER
PRIMARY EXAMINER

APPENDIX A

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RESULT 2
A57014
prostasin (EC 3.4.21.-) precursor - human
C;Species: Homo sapiens (man)
C;Date: 24-May-1996 #sequence_revision 24-May-1996 #text_change 21-Apr-2003
C;Accession: A57014; A54866
R;Yu, J.X.; Chao, L.; Chao, J.
J. Biol. Chem. 270, 13483-13489, 1995
A;Title: Molecular cloning, tissue-specific expression, and cellular localization of hum
A;Reference number: A57014; MUID:95286644; PMID:7768952
A;Accession: A57014
A;Status: translated from GB/EMBL/DDBJ
A;Molecule type: mRNA
A;Residues: 1-343 <RES>
A;Cross-references: GB:L41351; NID:g862304; PIDN:AAC41759.1; PID:g862305
A;Experimental source: prostate
A;Note: parts of this sequence were determined by protein sequencing
R;Yu, J.X.; Chao, L.; Chao, J.
J. Biol. Chem. 269, 18843-18848, 1994
A;Title: Prostasin is a novel human serine proteinase from seminal fluid. Purification,
A;Reference number: A54866; MUID:94308140; PMID:8034638
A;Accession: A54866
A;Molecule type: protein
A;Residues: 45-64 <YUA>
C;Genetics:
A;Gene: GDB:PRSS8
A;Cross-references: GDB:676446; OMIM:600823
A;Map position: 16p11.2-16p11.2
C;Superfamily: trypsin; trypsin homology
C;Keywords: glycoprotein; hydrolase; serine proteinase; transmembrane protein
F;1-32/Domain: signal sequence #status predicted <SIG>
F;33-44,45-343/Product: prostasin #status predicted <MAT>
F;33-44/Domain: prostasin light chain #status predicted <CHL>
F;45-343/Domain: prostasin heavy chain #status predicted <CHH>
F;45-281/Domain: trypsin homology <TRY>
F;323-341/Domain: transmembrane #status predicted <TMM1>
F;37-154,70-86,168-244,201-223,234-262/Disulfide bonds: #status predicted
F;85,134,238/Active site: His, Asp, Ser #status predicted
F;159/Binding site: carbohydrate (Asn) (covalent) #status experimental

  Query Match             14.1%;  Score 437.5;  DB 1;  Length 343;
  Best Local Similarity   35.3%;  Pred. No. 2.1e-23;
  Matches  110;  Conservative   48;  Mismatches  109;  Indels   45;  Gaps   14;

Qy        51 PQGKAKRHGNTVPGEWPWQASVRRQGAHICSGSLVADTWVLTAAHCFEKAAATELNSWSV 110
             ||  :     : | |:|||| |:  :| |:| |||::  |||:|||||      |  :: |
Db        41 PQARITGGSSAVAGQWPWQVSITYEGVHVCGGSLVSEQWVLSAAHCFPSEHHKE--AYEV 98


Qy       111 VLGSLQREGLSPGAEEVGVAALQ--LPRAYNHYSQGS--DLALLQLAHPTTHT----PLC 162
             ||: | :  |   |:  |: |:  :|   ::  :||  |:|||||: | | :    |:|
Db        99 KLGAHQLDSYS---EDAKVSTLKDIIPHP-SYLQEGSQGDIALLQLSRPITFSRYIRPIC 154

Qy       163 LPQPAHRFPFGASCWATGWDQDTSD----APGTLRNLRLRLISRPTCNCIYNQLHQRHLS 218
             ||     || |  |  |||           |  |: | : |||| ||||:||   :
Db       155 LPAANASFPNGLHCTVTGWGHVAPSVSLLTPKPLQQLEVPLISRETCNCLYNIDAKPEEP 214

Qy       219 NPARPGMLCGGPQPGVQGPCQGDSGGPVLCLEPDGHWVQAGIISFASSCAQEDAPVLLTN 278
             :  :  |:| |   | :  ||||||||: |   :| |   ||:|:  :|   : | : |
Db       215 HFVQEDMVCAGYVEGGKDACQGDSGGPLSC-PVEGLWYLTGIVSWGDACGARNRPGVYTL 273

Qy       279 TAAHSSWLQARV---QGAAFLAQSPETPEMSDEDSCVACGS-----------LR----- 318
             ::::||:|::|   |       |:| | |  || : |||            ||
Db       274 ASSYASWIQSKVTELQPRVV----PQTQE-SQPDSNL-CGSHLAFSSAPAQGLLRPILFL 327

Qy       319 TAGPQAGAPSPW 330
               |   |  |||
Db       328 PLGLALGLLSPW 339
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